Online Data Supplement

Sleep apnoea and lung cancer. Biomarkers of immune evasion, lymphangiogenesis and tumour cell aggressiveness

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Table S1. Comparison of biomarker levels between subjects with or without lung cancer*

	Non lung cancer (n=131)	**Lung cancer** (n=39)	**p-value**
TGF-ß, pg/ml	8.9 (5.5-12.0)	13.7 (12.4-17.6)	<0.001
SMAD3, pg/ml	2484 (1900-4594)	5087 (4581-5243)	<0.001
CD137, pg/ml	41.9 (6.0-41.9)	41.9 (6.3-82.4)	0.533
MMP2, pg/ml	17110 (12668-24309)	23460 (19445-27438)	<0.001
PSPC1, pg/ml	5087 (4581-5243)	2484 (1900-4594)	<0.001
MDK, pg/ml	1800 (703-4417)	4695 (4275-5757)	<0.001
PD-L1, pg/ml	43.1 (35.5-55.6)	61.3 (53.2-86.7)	0.001
PD-1, pg/ml	14.7 (6.1-25.5)	24.5 (13.5-43.4)	0.008
CTLA-4, pg/ml	2.03 (0.60-4.89)	0.60 (0.60-19.80)	0.883

*Data are median (interquartile range). Comparisons were performed by Mann-Whitney test.

Abbreviations: OSA, obstructive sleep apnoea; TGF-ß, transforming growth factor beta; SMAD3, SMAD family member 3; CD137, 4-1BB or tumour necrosis factor receptor superfamily 9; MMP2, matrix metalloproteinase-2; PSPC1, paraspeckle component 1; MDK, midkine; PD-L1, programmed death-ligand 1; PD-1, programmed cell death 1; CTLA-4, cytotoxic T-Lymphocyte Antigen 4.

Table S2. Risk factors associated with a diagnosis of lung cancer*

	Regression coefficient		Odds ratio		r^2	Change in r^2	p-value
	B	**Standard error**	**Value**	**95%CI**			
Desaturation index, h^{-1}	0.061	0.019	1.063	1.026-1.103	0.228	0.228	0.001
TGF-ß, pg/ml	0.054	0.029	0.056	0.997-1.118	0.268	0.040	0.063
Constant	-2.753	0.496	-	-	-	-	-

*Sex, BMI, pack-years, previous COPD diagnosis and all sleep parameters and biomarkers with significant differences in the bivariate analysis were included.

Abbreviations: B, regression coefficient; CI, confidence interval; r^2, coefficient of determination; TGF-ß, transforming growth factor beta.

Figure S1. Relationship between serum levels of PSPC-1, MDK, PD-L1 and PD-1 with desaturation index in subjects from the SAILS cohort. r values correspond to Pearson correlation coefficients.

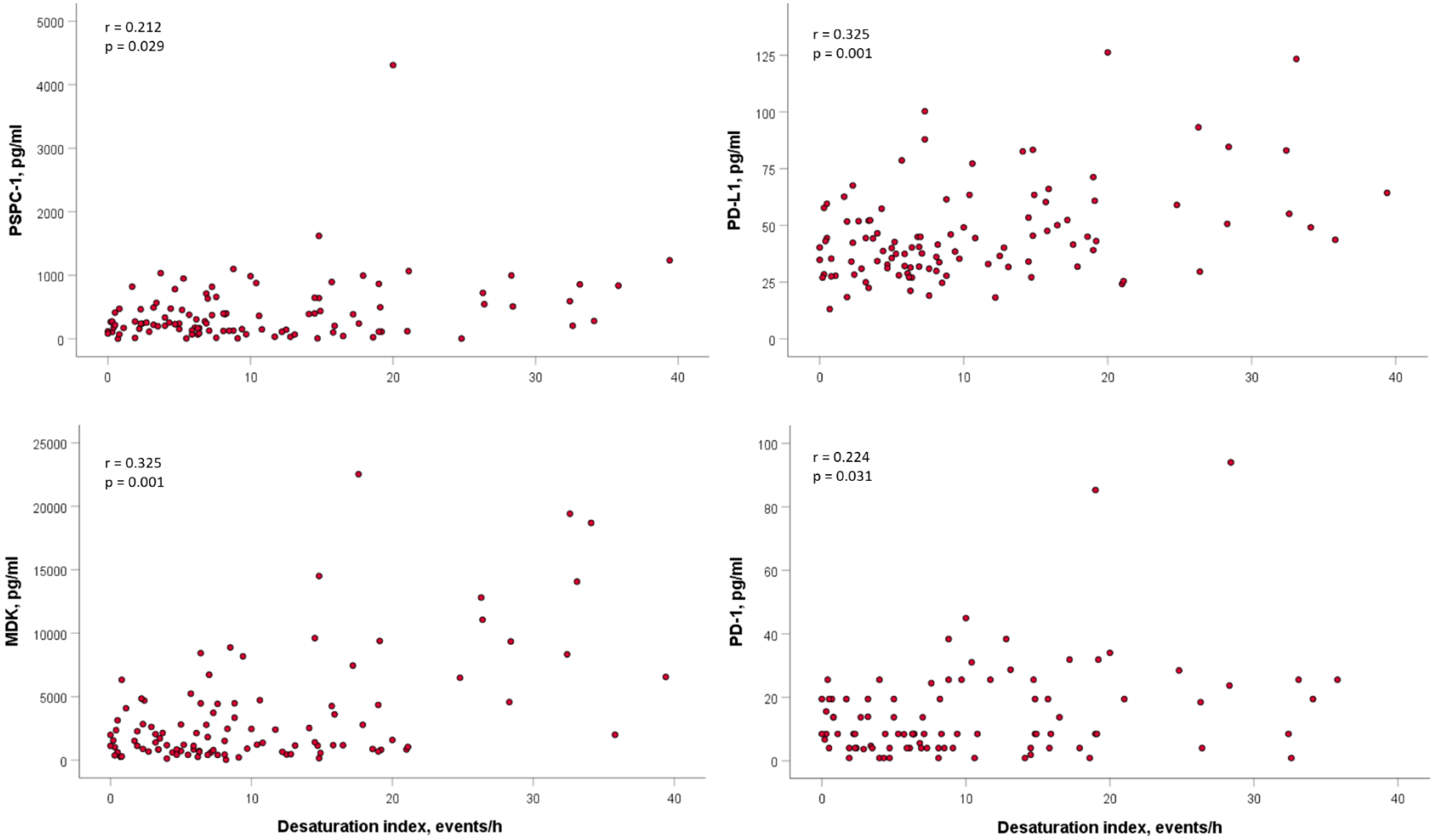


Figure S2. Relationship between serum levels of PSPC-1, MDK and PD-L1 with minimum saturation in subjects from the SAILS cohort. r values correspond to Pearson correlation coefficients.

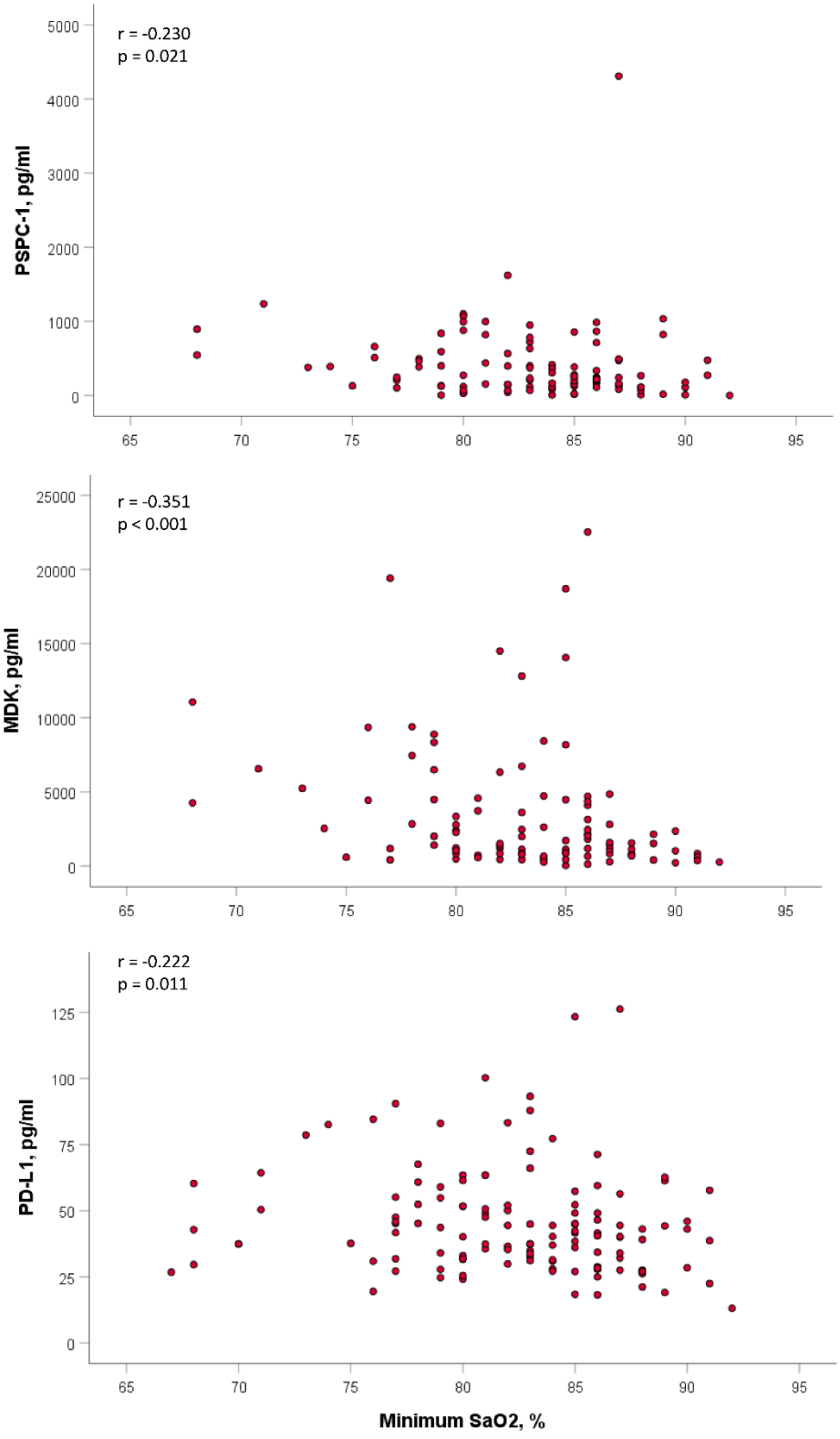


Figure S3. Relationship between serum levels of PSPC-1, TGFß1 and PD-L1 with mean saturation in subjects from the SAILS cohort. r values correspond to Pearson correlation coefficients.

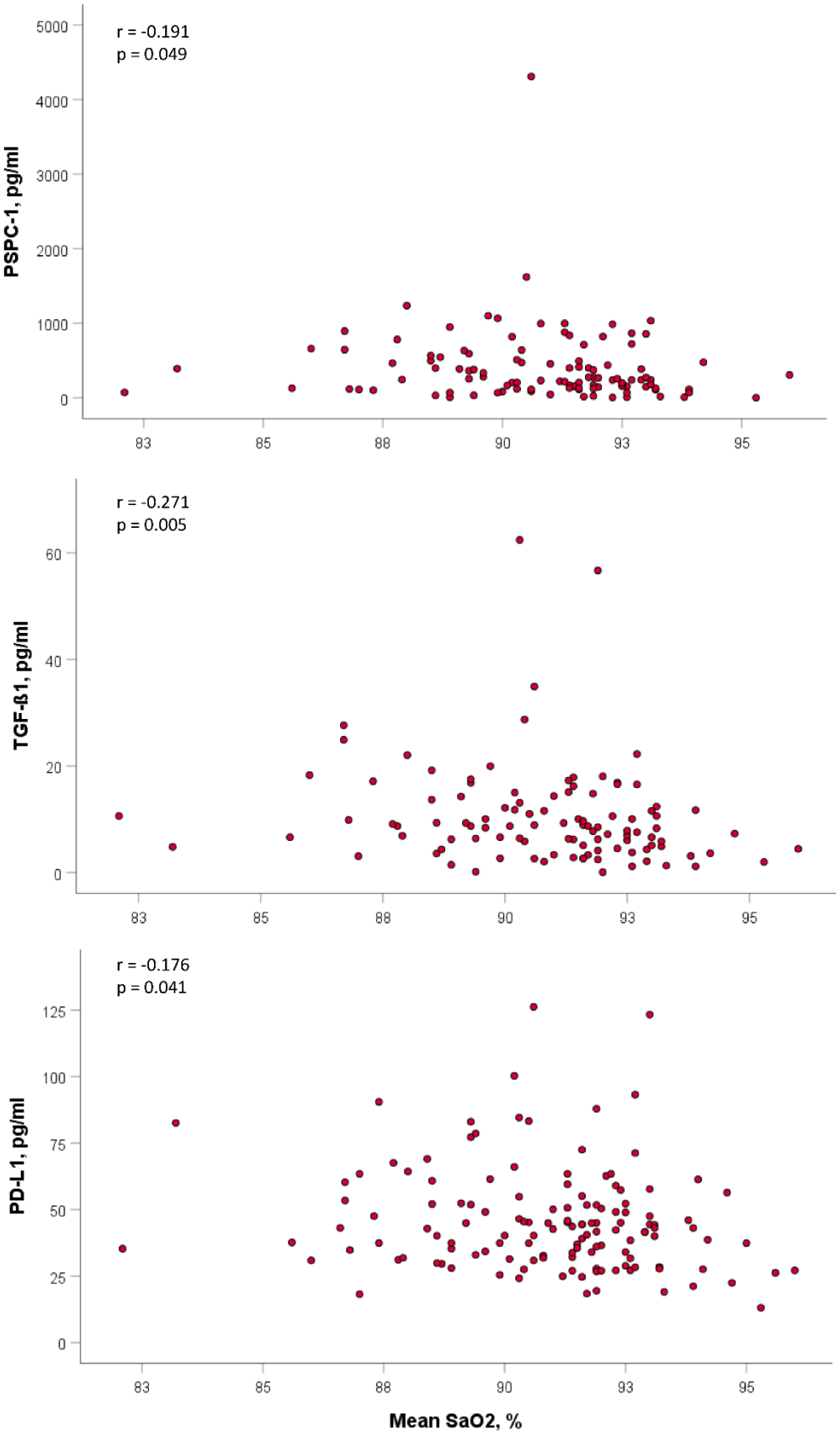

r = -0.191
p = 0.049
PSPC-1, pg/ml
5000
4000
3000
2000
1000
0
83
85
88
90
93
95
r = -0.271
p = 0.005
TGF-ß1, pg/ml
60
40
20
0
r = -0.176
p = 0.041
PD-L1, pg/ml
125
100
75
50
25
0
Mean SaO2, %

Figure S4. Relationship between serum levels of PSPC-1, TGFß1 and PD-L1 with recording time with oxyhaemoglobin saturation less than 90% in subjects from the SAILS cohort. r values correspond to Pearson correlation coefficients.

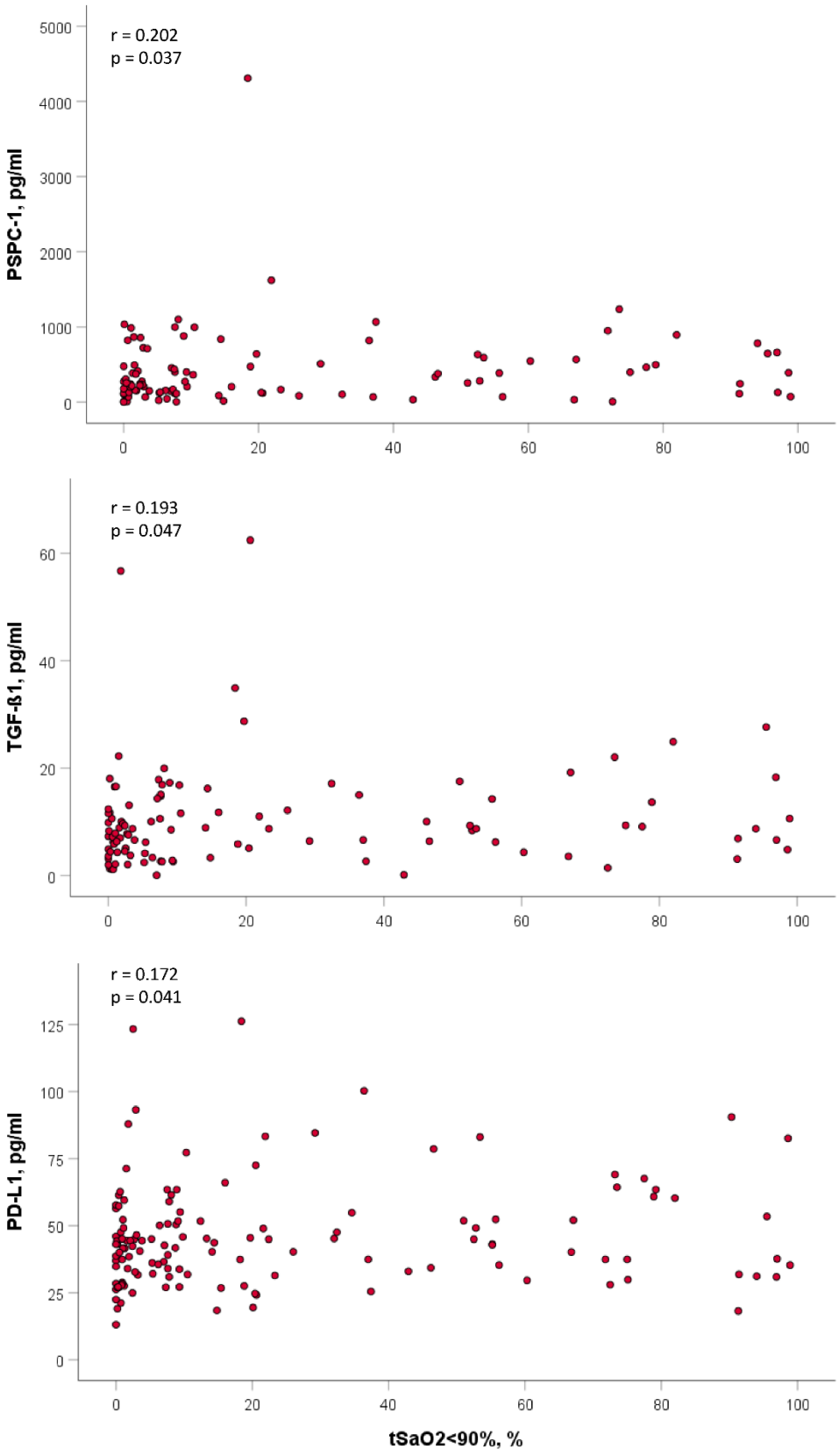


Figure S5. Relationship between serum levels of PSPC-1, TGF-ß1, PD-L1 and PD-1 with desaturation index in subjects from the SAIL cohort. r values correspond to Pearson correlation coefficients.

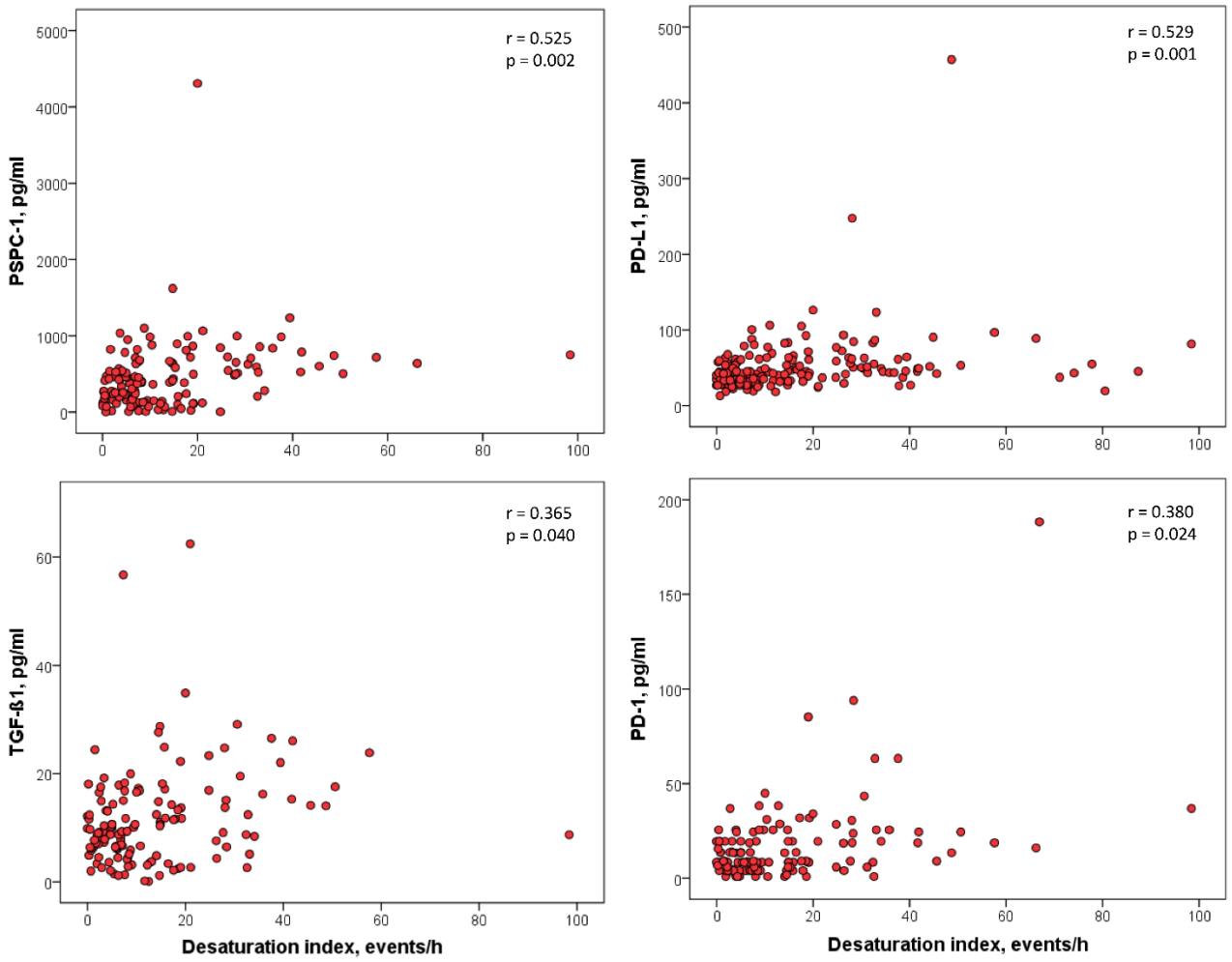
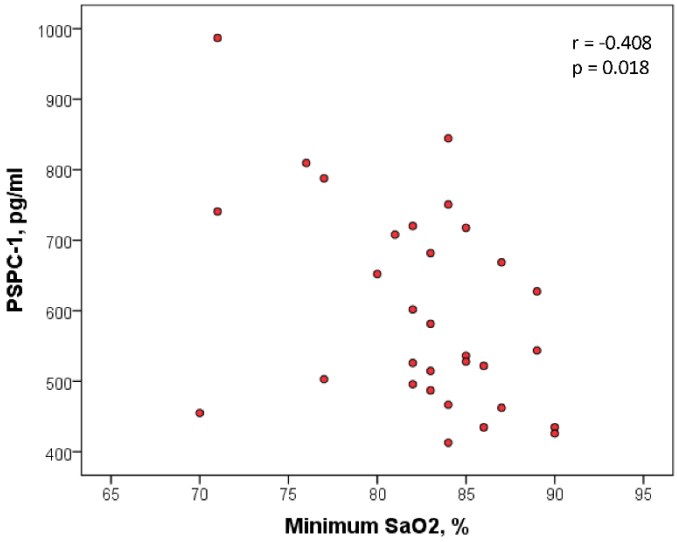
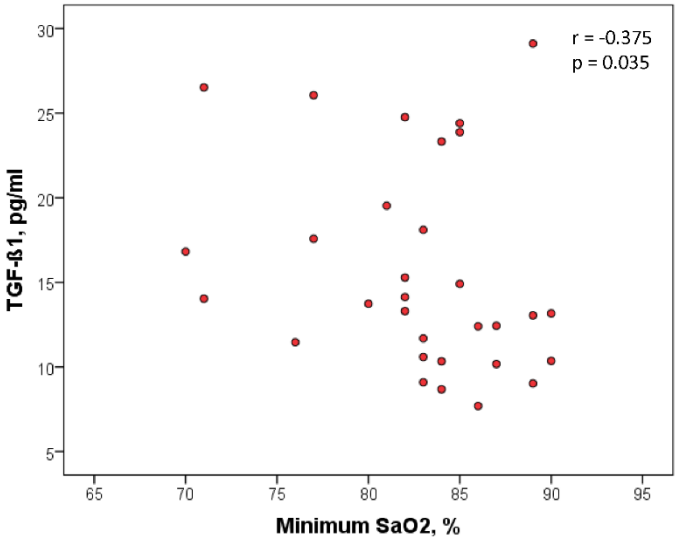
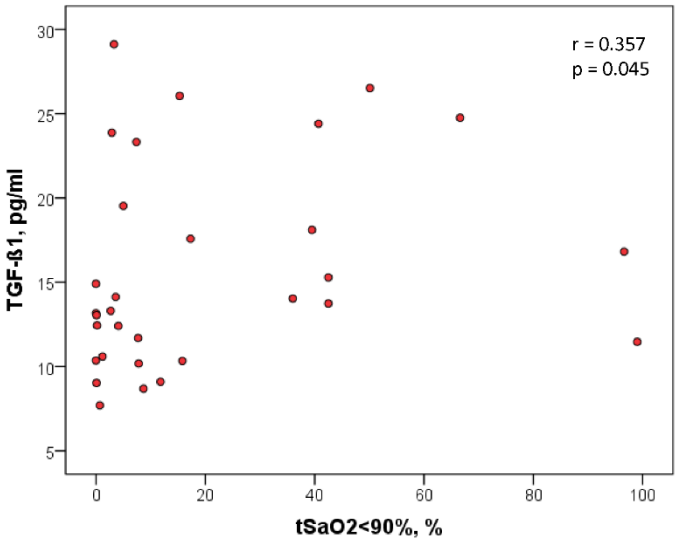


Figure S6. Relationship between serum levels of PSPC-1 and TGF-ß1 with other hypoxemic indices in subjects from the SAIL cohort. r values correspond to Pearson correlation coefficients.


r = -0.408
p = 0.018
PSPC-1, pg/ml
1000
900
800
700
600
500
400
65
70
75
80
85
90
95
Minimum SaO2, %


r = -0.375
p = 0.035
TGF-ß1, pg/ml
30
25
20
15
10
5
65
70
75
80
85
90
95
Minimum SaO2, %


r = 0.357
p = 0.045
TGF-ß1, pg/ml
30
25
20
15
10
5
0
20
40
60
80
100
tSaO2<90%, %